REMARKS

Claims 11-24 and 28-54, and claims 1-10 and 25-27 are cancelled herein without prejudice to their patentability. New claims 55-75 are added. Upon entry of this amendment claims 55-75 will be pending. Applicants have removed the embedded hyperlinks found in the first and fourth paragraphs of page 21, thereby complying with MPEP § 608.01. Attached hereto is a marked-up version of the changes made to the specification by the current amendments. The attached page is captioned "**Version With Markings to Show Changes Made.**"

Support for new claims 55-75 may be found beginning at page 14, line 27 through page 18, line 2, wherein the process of preparing sporulated oocysts, disrupting the oocyst walls, and formulating vaccine preparations is disclosed. Additional support for claims 55-75 may be found on page 18, line 3 through page 22, line 2 which describe testing for bacterial, fungal, and viral contamination. Further support for claims 55-65 and 67-68 may be found at page 15, lines 27-28, which indicates that washing may be accomplished by tangential flow filtration. Support for claims 59, 60, 69, and 70 can be found on page 22, line 19 to page 23, line 7, which gives dosage amounts for sporocysts. Support for claims 61 and 71 can be found on page 24, line 22 to page 25, line 2 which describe useful preservatives. Support for claims 62 and 72 can be found on page 25, lines 3-21, which describe immune system stimulants. Support for claims 63 and 73 can be found on page 25, lines 22-31, which describe vaccine preparations for at least one additional disease of birds. Support for claims 64 and 74 can be found on page 26, lines 1-11, which describe growth stimulants.

Rejection of Claims 1-10 and 25-27 under 35 U.S.C. § 112

The Office has stated that claims 1-10 and 25-27 are indefinite because the term "substantially free" is not defined by the claim and a standard for ascertaining the requisite degree is not provided by the specification. Claims 1-10 and 25-27 have been cancelled, and new claims 55-75 have been added. The new claims are directed to "sterile" preparations, and do not contain the term "substantially free." In support of the term "sterile," the specification indicates that the vaccine preparation is sterilized, see p. 15, ln. 20-21, and describes several methods of testing for extraneous viable bacteria, fungi, and viruses that affect birds. *See* Specification, p. 18, ln. 3 through p. 22, ln. 2. Standards are also given for acceptable levels of bacterial and fungal contamination (p. 18, ln. 28 to p. 19, ln. 2), Salmonella (p. 19, ln. 16-17), Chick Anemia Virus (p. 20, ln. 16-18 and p. 21, ln. 7-9), and Infectious Bursal Disease Virus (p. 21, ln. 23-25 and p. 21, ln. 31 to p. 22, ln. 2). As such, the specification clearly provides a standard for ascertaining the requisite degree of sterility. Thus, the basis for the Office's objection to the specification on the basis of 35 U.S.C. §112, second paragraph, has been removed.

Rejection of Claims 1-6, 8-10, 25, and 27 under 35 U.S.C. §102(b)

The Office has rejected claims 1-6, 8-10, 25, and 27 under §102(b) as anticipated by Evans, et al. (WO 96/40233). Claims 1-6, 8-10, 25, and 27 have been cancelled, and new claims 55-75 have been added.

New claims 55-65 are directed to preparations for the treatment of coccidiosis in members of the class *Aves* comprising live sporocysts of at least one species of coccidial protozoa, a

pharmaceutically acceptable carrier, diluent, or excipient, and wherein the preparation is sterile, and is filtered by tangential flow filtration.

New claims 66 to 75 are directed to sterile preparations for treatment of coccidiosis in members of the class *Aves* comprising live sporocysts of the species *E. tenella, E. maxima,* and *E. acervulina*. The latter compositions also comprise a pharmaceutically acceptable carrier, diluent, or excipient.

Evans discloses a method for the *in ovo* vaccination of domesticated birds against coccidiosis using live *Eimeria* sporocysts, oocysts, or a mixture thereof. Evans further discloses a preferred dose of from 10^2 to 10^8 sporocysts per egg (page 6, lines 25-30) or 10^2 to 10^8 oocysts per egg (page 6, lines 8-10), and indicates that such sporocysts or oocysts may be from two or more species of *Eimeria*, including the species *E. tenella, E. acervulina, E. maxima, E. necatrix, E. mitis, E. praecox,* and *E. brunetti*. The use of suspending agents and immune stimulants in combination with the vaccine compositions are also disclosed.

However, Evans does not provide for nor suggest tangential flow filtration of the vaccine composition, as required by claims 55-65; nor does Evans provide guidance as to the level of sterility of the vaccine. Evans simply indicates that the oocyst suspension is incubated in sodium hypochlorite at room temperature for 15 minutes (p. 6, ln. 16-17). While disclosing a list of multiple species of *Eimeria*, Evans fails to teach or suggest the specific combination of *E. tenella, E. maxima,* and *E. acervulina*, as specified in claims 66-75. Consequently, the claims of the present invention are not anticipated by Evans.

Rejection of Claims 1-10, and 25-27 under 35 U.S.C. §103 (a)

The Office has rejected claims 1-10 and 25-27 as being unpatentable over Evans in view of MacDonald, et al. (U.S. Pat. No. 5,055,292) as applied to claims 1-10 and 25 and 27, and as being unpatentable over Evans in view of MacDonald as applied to claims 1-10 and 25 and 27 and further in view of Rolinski, et al. (Medycyna Weterynaryjna, 44(8):abstract 1988) or Thaxton (U.S. Pat. No. 5,311,841). Claims 1-10 and 25-27 have been cancelled, and new claims 55-75 have been added.

For a combination of references to render obvious a claimed invention, the Office must show: (1) some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) a reasonable expectation of success; and (3) that the prior art reference (or references when combined) teach or suggest all the claim limitations. MPEP § 2143. This showing has not been made.

The Office has stated that Evans differs from the claimed vaccine composition in that the addition of preservatives to the vaccine composition is not taught. The Office further states that MacDonald teaches "that it is desirable to add preservatives to vaccines to inhibit contamination with other organisms," and that it would thus be *prima facie* obvious to add a preservative according to MacDonald to the *in ovo* vaccine composition of Evans.

However, as previously discussed, Evans differs from the present claims in more ways than just the absence of preservatives. Evans does not disclose the filtration of the vaccine by tangential flow filtration as specified in claims 55-

65, does not provide guidance as to sterility levels, and does not disclose or suggest the particular combination of *E. tenella*, *E. maxima*, and *E. acervulina* as called for in claims 66-75.

MacDonald discloses a vaccine containing live sporulated oocysts, and does discloses the combination of *E. tenella*, *E. maxima*, and *E. acervulina*, but mentions nothing about the use of tangential flow filtration to filter the vaccine. In fact, the vaccine composition in Example 1 of MacDonald is not even "washed" after treatment with sodium hypochlorite solution, but rather is only resuspended in water, with formalin added. Furthermore, MacDonald does not provide guidelines as to the level of sterility of the vaccine. The mere fact that MacDonald suggests the desirability of adding a preservative to the composition does not provide a "suggestion or motivation" to modify the composition of Evans in the manner required by the claims of the present invention. As such, Applicants submit that claims 55-75 are patentable over Evans in view of MacDonald.

Rolinski is cited for teaching the minimum inhibitory concentration of gentamicin for common Salmonella strains isolated from animal and poultry. Thaxton is cited by the Office for disclosing the delivery of medicaments to newly hatched poultry via intra-yolk sac injection, and the use of gentamicin "to prevent or retard early bacterial infection, to promote early growth, and reduce post-hatching stress."

As stated above, the combination of Evans and MacDonald does not teach or suggest each claim limitation, in particular, the combination does not teach or suggest the use of tangential flow filtration to filter the vaccine composition, nor do they provide standards of sterility with regards to bacterial, fungal, and viral contaminants. Neither Rolinski nor Thaxton suggest the

modification of Evans in view of MacDonald to encompass these features of the present claims.

Based on the foregoing, Applicants respectfully submit that claims 55-75 are patentable over Evans in view of MacDonald and/or Rolinski or Evans in view of MacDonald and/or Thaxton.

VERSION WITH MARKINGS SHOWING CHANGES MADE

IN THE SPECIFICATION

The paragraph beginning on line 1 of page 21 has been amended as follows:

Conserved regions of the Chicken Anemia Virus viral genome are amplified using standard techniques (Innis et al., *PCR Protocols*, Academic Press, 1990). Information on the Chicken Anemia Virus viral genome for designing suitable primers can be found on databases well known to those in the biomedical arts such as the databases available through the **website of the** U.S. National Institutes of Health **[website at http://www.ncbi.nlm.nih.gov, all herein incorporated by reference]**. PCR products are analyzed by agarose gel electrophoresis and ethidium bromide staining. If the PCR amplification does not result in a band corresponding to the band found in the positive control, the preparation is considered substantially free of Chicken Anemia Virus.

The paragraph beginning on line 26 of page 21 and continuing on page 22 is amended as follows:

Alternatively, the test for the IBDV contamination can be accomplished using PCR as described for Chicken Anemia Virus. Information on the IBDV viral genome for designing suitable primers can be found on databases well known to those in the biomedical arts such as the databases available through the **website of the** U.S. National Institutes of Health **[website at http://www.ncbi.nlm.nih.gov, all herein incorporated by reference]**. If the PCR amplification does not result in a band corresponding to the band found in the positive control, the

preparation is considered substantially free of Infectious Bursal Disease Virus.

IN THE CLAIMS

Claims 11-24 and 28-54, and claims 1-10 and 25-27 have been canceled.

Claims 55-75 are new.

CONCLUSION

In light of the foregoing, Applicants request entry of the new claims, and favorable consideration of the application.

The Commissioner is hereby authorized to charge to Deposit Account No. 19-1345 any additional fees under 37 C.F.R. 1.16 and 1.17 which may be required during the entire pendency of this application.

Respectfully submitted,

Anthony R. Kinney, Reg. No. 44,834
SENNIGER, POWERS, LEAVITT & ROEDEL
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
(314) 231-5400

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